Case Report

Chyliform effusion without pleural thickening in a patient with rheumatoid arthritis: A case report

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ABSTRACT

Pseudochylothorax, also known as chyliform effusion rich in cholesterol crystals, is a rare entity that sometimes occurs in long-standing rheumatoid arthritis (RA) and is usually associated with thickened pleura. There have only been a few case reports in the literature on pseudochylothorax unassociated with pleural thickening and with a short duration of articular symptoms in patients with RA. We report the case of a 70-year-old male patient with a history of RA and heart failure due to severe aortic stenosis, who presented with signs and symptoms of decompensated heart failure due to a moderate right-sided pleural effusion that was consequently proved to be pseudochylothorax unassociated with pleural thickening on chest computed tomography (CT) scan. The patient's outcome was favorable after thoracocentesis was carried out and leflunomide was added to the standard heart failure treatment.

KEY WORDS: Cholesterol crystal, chyliform effusion, pseudochylothorax, rheumatoid arthritis, thickened pleura

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INTRODUCTION

Pleural effusion with a high level of cholesterol, known as pseudochylothorax or chyliform effusion is often encountered in patients with tuberculosis. It is a relatively rare finding in patients with rheumatoid arthritis (RA) where it can be found in up to 5% of cases.[1] Other rare causes of pseudochylothorax are pleural paragonimiasis, trauma, and therapeutic pneumothorax.[2]

Currently there are only a few cases in the literature describing RA-associated chyliform effusion. It may rarely occur in patients with a long history of RA and occasionally appears during or even precedes the onset of articular symptoms.[3-5]

In most cases, thickening of the pleura with pleural effusion is encountered.[2] Pleural thickening may be detected on the chest computed tomography (CT) scan as a layer of tissue density between the chest wall and lungs, with a thickening of more than 1 cm being a sign of malignancy.[6] We report a case of pseudochylothorax diagnosed by thoracocentesis in a patient with a history of inconsistently treated RA and heart failure due to severe aortic stenosis, unassociated with pleural thickening on chest CT scan.

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CASE REPORT

A 70-year-old nonsmoking male patient, with a 22-year history of RA, arterial hypertension, severe aortic stenosis and heart failure, was admitted to our department for the rapid onset of severe dyspnea and cough in the past 3 days. His medication at home consisted of a beta blocker, diuretic, nitrate, angiotensin-converting-enzyme inhibitor (ACE-inhibitor), statin and platelet inhibitor but no medication for RA.

The physical examination revealed following data: Blood pressure of 160/90 mmHg, heart rate of 104 bpm, oxygen saturation of 88%, body temperature 36.9°C, signs of right pleural effusion and diffuse bronchial rales, systolic murmurs in the mitral and aortic valve areas, perioral cyanosis and no peripheral edema. The patient presented with symmetrical rheumatoid deformities of the hands

with ulnar deviation, "swan neck" fingers, without signs of active arthritis but with impaired mobility and rheumatoid nodules on the elbows.

Blood sample tests showed mild inflammatory anemia, decreased renal function (creatinine clearance of 33 mL/min/1,73 m^2), and normal values (NVs) of the serum electrolytes and liver function tests. The C-reactive protein (9.3 mg/dL, NV <1 mg/dL), erythrocyte sedimentation rate (95 mm/h, NV: 0-20 mm/h), and fibrinogen levels (682.2 mg/dL, NV: 200-400 mg/dL) were elevated. The serum triglycerides and total cholesterol levels were normal at 85 mg/dL and 139 mg/dL, respectively. The N-terminal pro-B-type natriuretic peptide (NT-proBNP) level was elevated (2498.88 pmol/L, NV: <35.4 pmol/L). Arterial blood gas analysis revealed normal pH, hypocapnia, and moderate hypoxemia (56.3 mmHg, NV: 83-108 mmHg).

The chest x-ray described the accentuation of Kerley A and B lines, reticular interstitial infiltrates, cardiomegaly, and a moderate right pleural effusion [Figure 1]. The standard electrocardiogram showed sinus rhythm and left ventricular hypertrophy.

Treatment with loop diuretics, oxygen, and bronchodilators was initiated. Thoracocentesis was carried out and 900 ml of turbid, yellow fluid was evacuated [Figure 2]. Biochemical analysis of the fluid demonstrated an exudative nature: Total proteins 7.87 mg/dL, lactate dehydrogenase (LDH) 1122 U/L, pleural LDH/serum LDH ratio of 3.25, cholesterol 148 mg/dL, triglycerides 41 mg/dL, and glucose 59 mg/dL (NV: 70-110 mg/dL). A low level of complement C3 and C4 at 0.04 g/L and 0 g/L, respectively, was also noted. On microscopic examination, cholesterol crystals were observed [Figure 3]. Microbiological smears and cultures were negative, including for *Mycobacterium tuberculosis*.

The chest CT scan carried out after thoracocentesis revealed a mild right-sided pleural effusion but without pleural thickening and several bands of atelectasis [Figure 4]. No lung tumor, evidence of pulmonary tuberculosis, or

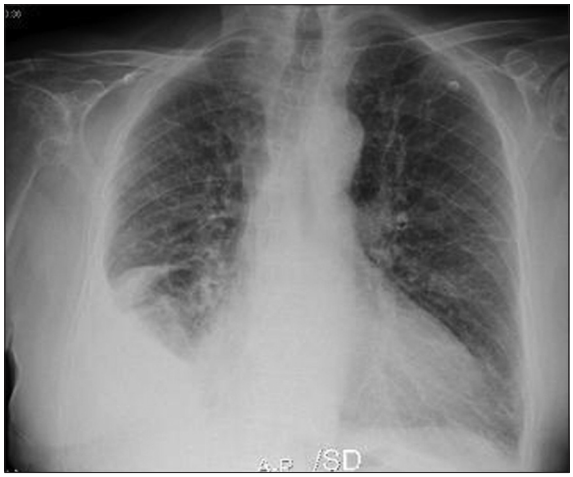

Figure 1: Chest radiography with right pleural effusion

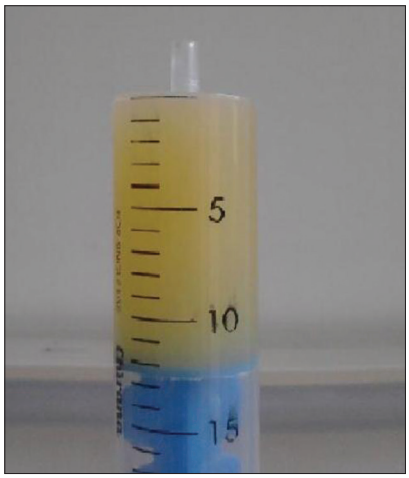

Figure 2: Macroscopic examination of the pleural fluid revealing an opalescent and turbid liquid

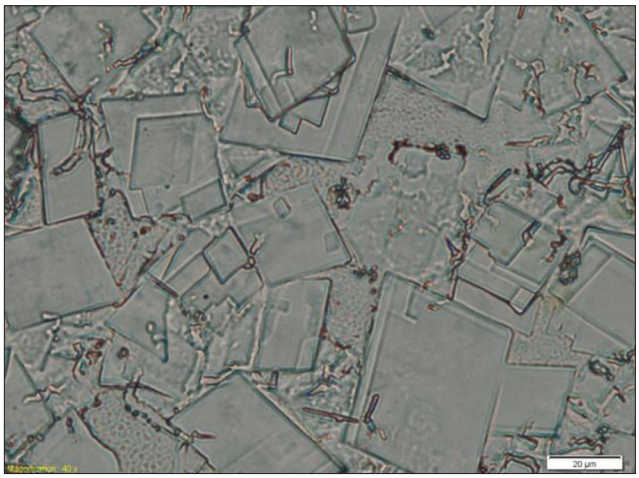

Figure 3: Optical microscopy showing cholesterol crystals (40X magnification)

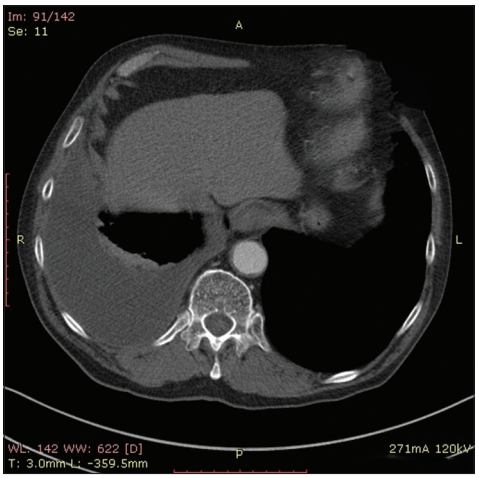

Figure 4: Chest CT scan showing pleural effusion without thickening of the pleura

mediastinal lymph node was observed. However, due to the presence of advanced heart failure, thoracoscopy was not carried out for definitive diagnosis.

The course of the disease was favorable and the patient was discharged with leflunomide 20 mg/day associated with heart failure treatment.

DISCUSSION

This report describes a case of pseudochylothorax in a patient with heart failure due to severe aortic stenosis and a long history of RA, occurring in the absence of typical thickened pleura. To our knowledge, there have been very few cases describing RA-associated chyliform effusion with rapid onset of articular symptoms and without pleural thickening.[5]

The pathophysiology of this condition is incompletely understood. One theory suggests that pseudochylothorax can only develop in the presence of thickened pleura, requiring the persistence of pleural inflammation for at least 5 years.[2] It is assumed that the presence of cholesterol in the pleural space is a result of the degradation of erythrocytes and neutrophils. Nevertheless, Wrightson *et al*. demonstrated that the presence of cholesterol in the pleural space may also be due to an acute process.[5] Another theory, the "general metabolic theory," suggests that the presence of cholesterol in the pleural fluid is the result of an elevated level of serum cholesterol. However, in patients with pseudochylothorax, the level of serum cholesterol is usually normal[7] that was also the case in our patient.

The diagnosis of pseudochylothorax is based on the biochemical and microscopic analysis of the pleural fluid. It is a type of exudate characterized by an elevated level of cholesterol (≥200 mg/dL) and a low level of triglycerides (<110 mg/dL),[4] glucose and complement components' activity.[8] On microscopic examination, cholesterol crystals are recognizable by their typical aspect of rectangular plates with indented edges.[7] In our case, the level of pleural cholesterol was less than 200 mg/dL but the pleural/serum cholesterol ratio >1 and the presence of cholesterol crystals on the microscopic examination support the diagnosis of chyliform effusion.

An important diagnostic tool for the evaluation of chyliform pleural effusion is the CT scan. This imaging technique can show thickening of the parietal and visceral pleura or loculated pleural collection, which suggest a long duration of the inflammatory process. Other possible findings include nodular and linear calcifications of the pleura. Song *et al*. found a fat-fluid and fat-calcium levels in six patients with a long history of chyliform effusion (5 patients with tuberculous pleural effusion and one patient with pleura-pulmonary paragonimiasis).[9] These modifications are considered unique features in chyliform effusion.[9] In our case, none of these modifications described above were observed on CT scan.

Thoracoscopy is not usually performed in typical cases of RA-related pseudochylothorax. However, it may be considered when a definitive diagnosis is important, such as in the cases of malignancies or in atypical cases.[10] It allows fluid analysis, cellularity assessment, pleural cavity inspection and sampling of pleural biopsies. In our case, thoracoscopy was not performed due to the procedure-associated risks in a patient with advanced heart failure.

Wrightson *et al*. found no pleural thickening in six patients with arthritis-related pseudochylothorax with short duration of RA, suggesting that chyliform effusion should be taken into consideration even in cases with minimal pleural involvement.[5] Pleural thickening was evaluated in these cases using CT scan and thoracoscopy in three patients.

The course of RA-related cholesterol pleurisy is variable and its treatment is not well established. Available data show that in patients with small, asymptomatic effusions, specific treatment is not necessary. In cases with large effusions, treatment consists in repeated thoracocentesis and intrapleural instillation of corticosteroids, but the results are variable.[8,11] In some cases, the administration of nonsteroidal anti-inflammatory drugs is sufficient but sometimes systemic corticotherapy or the addition of another antirheumatic drug may be necessary.[5,11,12] The persistence of pleural effusion may favor the development of thickened pleura, trapped lung, and infection.[12] In cases with persistent effusion and pleural thickening, decortication may be necessary but with an increased risk of morbidity and mortality.[13]

The patient presented in this case report had a long history of RA and neglected treatment; thus, RA was only moderately active, with a DAS28 score of 4.2 [on account of an elevated C-reactive protein CRP level]. The patient only had knee pain, estimated at 45 out of 100 without swelling, rheumatoid hands with deformities (ulnar deviation, "swan neck" fingers), and impaired mobility. Therefore, the patient was considered to have "burned out" RA with systemic manifestations, with no indication for systemic NSAIDs therapy. The initiation of systemic corticosteroid therapy was not possible due to the presence of heart failure. Intrapleural glucocorticoids were not used due to the lack of compelling results.

This case suggests that when pleural effusion is detected in patients with heart failure and concomitant RA, one should think of the possibility of chyliform effusion even though it is a rare finding. Also, in patients with RA-related chyliform effusion without pleural thickening, the lack of a grossly elevated level of intrapleural cholesterol might be an earlier finding preceding the development of pleural thickening.

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